

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 4649-4002PC		Date of mailing (day/month/year) 10 MAY 2006 FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US05/07524	International filing date (day/month/year) 03 March 2005 (03.03.2005)	Priority date (day/month/year) 03 March 2004 (03.03.2004)
International Patent Classification (IPC) or both national classification and IPC IPC(8): A61K 51/00(2006.01);A61K 39/40(2006.01);A61K 39/42(2006.01) USPC: 424/1.21,1.25,1.29,1.33,1.53,236.1,239.1,247.1		
Applicant ESSENTIA BIOSYSTEMS, INC.		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

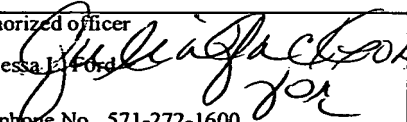
2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 03 April 2006 (03.04.2006)	Authorized officer  Vanessa L. Ford Telephone No. 571-272-1600
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Form PCT/ISA/237 (cover sheet) (April 2005)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US05/07524

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
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International application No.
PCT/US05/07524

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-150</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-150</u>	NO
Industrial applicability (IA)	Claims <u>1-150</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-6, 12-16, and 19-48 lack novelty under PCT Article 33(2) as anticipated by CROSLAND ET AL. (The Journal of Histotechnology, Vol. 22, No. 2, June 1999). CROSLAND ET AL, teach compositions comprising botulinum toxin A and a carrier (latex microspheres). See the entire document. Thus, CROSLAND ET AL teach the claimed invention.

Claims 1-10, 12 and 19-48 lack novelty under PCT Article 33(2) as anticipated by SHALABY (Crisp Data Base National Institutes of Health, STN database 2002). SHALABY teaches compositions comprising botulinum toxin A-G and polymers. See the Abstract. Thus, SHALABY teaches the claimed invention.

Claims 1-150 lack inventive step under PCT Article 33(3) over SCHANTZ ET AL (Microbiological Reviews, March 1993, p. 80-99) in view of SHALABY and further in view of CONSOLE ET AL (The Journal of Biological Chemistry, Vol. 276, No. 37, September 12, 2003). SCHANTZ ET AL teach that botulinum toxins can be used in medical applications (pages 83-84.). SHALABY ET AL teach the botulinum toxin can be conjugate to polymers. CONSOLE ET AL teach that botulinum toxin can be used to deliver drugs or compounds to target sites. See the entire document.